Chapter-2

Review of Literature

2.1 Endophytic bacteria

Bacteria that invade the internal tissue of the host plant showing no external sign of infection or adverse effects on their host are termed as "endophytic bacteria". Endophytic bacteria play a crucial role in increasing plant biomass, cadmium uptake, nitrogen fixation, and phytohormone production. Therefore, they were found widely distributed in most of the plants (Chen *et al*., 2014; Khan *et al*., 2014).

Endophytic bacteria with plant growth-promoting factors were studied by Jasim *et al*., (2013) from *Piper nigrum* that resulted in the identification of *Klebsiella* sp. (PnB 10) and *Enterobacter* sp. (PnB 11) with properties like phosphate solubilization, ACC deaminase, and siderophore production. Aswathy *et al*., (2013), in their work noticed the indole 3 acetic acid (IAA) production of two endophytic species of *Paenibacillus* in the rhizome of *Curcuma longa*. Different strains of endophytic bacteria were isolated from a ginger rhizome by Jasim *et al*., (2014a), in which *Pseudomonas* sp. can produce IAA, ACC deaminase, and siderophore. In another work, Jasim *et al*., (2014b) studied endophytic *Pseudomonas aeruginosa* from ginger having an inhibitory effect on the fungus *Pythium myriotylum*.

Through in vitro propagation, Jimitha *et al*., (2014) isolated endophytic bacteria such as *Ralstonia* sp. and *Bacillus* sp. from suspension cultures of banana somatic embryos. These bacterial strains solubilize phosphate and produce indole acetic acid, siderophore, and ammonia. Liu *et al*., (2018) isolated endophytic bacteria from *Morinda citrifolia* L. fruits, and was identified as *Paenibacillus polymyxa* 19 using MALDI-TOF Mass Spectrometry. The strain shows suitable antagonistic property against smut pathogen *Aspergillus aculeatus* 23 NP-1, which was proved by acquiring the draft genome of *Paenibacillus* sp. NEB by Illumina HiSeq 2000 sequencing platform resulting in the annotation of three coding sequences for glucanases. Another species of *Paenibacillus* (*P. polymyxa* CICC10580) were identified by Xu *et al.*, (2014) from *M. citrifolia* fruits which have good antagonistic activity against many pathogens, and the coding sequences (CDSs) related with antagonism were annotated. Kumala and Siswanto (2007), in their work, also have isolated five bacterial isolates and eleven fungal isolates from *M. citrifolia* and studied broad-spectrum antifungal activity against *Candida albicans*.

Table no. 2.1 Some common endophytic bacterial species from the agronomic plant.

Bacteria	Host	References
Bacillus sp.	Papaya,	Krishnan *et al.*,2012
	Coffee,	Miguel *et al.*,2013
	Cucumber	Mahaffee and Kloepper, 1997
	Strawberry,	Pereira *et al.*,2012
	Black pepper	Aravind *et al.*, 2009
	Paddy, Maize, Cucumber, Hybrid spruce, Pine, Potato, Red clover.	Chanway, 1998
	Wheat	Tian *et al.*, 2017
	Mulberry	Ji *et al.*, 2008
	Potato	Hollis, 1951
		De Boer and Copeman, 1974
	Sugar beet	Jacobs *et al.*, 1985
	Rambutan	Suhandono *et al.*, 2016
	Jojoba	Elvia *et al.*, 2017
	Grapevine	Bell *et al.*, 1995

	Citrus	Araujo *et al*., 2001
	Canola and Wheat	Germida *et al*., 1998
	Red clover	Sturz *et al*., 1998
	Cotton	McInroy and Kloepper, 1995
		Misaghi and Donndelinger, 1990
	Rice	Stolzfus *et al*., 1997
		Bacilo-Jimenez *et al*., 2001
	Maize	Riggs *et al*., 2001
	Rough lemon	Gardner *et al*., 1982
	Corn	Lalande *et al*., 1989
Corynebacterium sp.	Maize, Potato, Lemon, Beet	Chanway, 1998
	Rambutan	Suhandono *et al*., 2016
	Rough lemon	Gardner *et al*., 1982
	Corn	Lalande *et al*., 1989
	Rice	Bacilo-Jimenez *et al*., 2001
Chryseobacterium sp.	Corn	Liu *et al*., 2012
	Sugar beet	Jacobs *et al*., 1985
	Rambutan	Suhandono *et al*., 2016
	Paddy, Coffee	Miguel *et al*., 2013
	Cucumber	Chanway, 1998
		Mahaffee and Kloepper, 1997
Azospirillum sp.	Rice	Stolzfus *et al*., 1997
	Maize	Riggs *et al*., 2001
Lactobacillus sp.	Sugar beet	Jacobs *et al*., 1985
Agrobacterium sp.	Rice	Stolzfus *et al*., 1997
	Cucumber	Mahaffee and Kloepper, 1997
	Potato	De Boer and Copeman, 1974
	Cotton	Misaghi and Donndelinger, 1990
Klebsiella sp.	Red clover	Sturz *et al*., 1998
	Grapevine	Bell *et al*., 1995

	Arabidopsis	Dong *et al.*, 1994
	Corn	Fischer *et al.*, 1992
	Wheat	Iniguez *et al.*, 2004
		Dong *et al.*, 1994
	Alfalfa	Dong *et al.*, 1994
	Rice	Elbeltagy *et al.*, 2000
		Dong *et al.*, 1994
Staphylococcus sp.	Maize	Liu *et al.*, 2012
	Vitis sp.	Collins *et al.*, 2004
	Rambutan	Suhandono *et al.*, 2016
	Grapevine	Bell *et al.*, 1995
	Cotton	McInroy and Kloepper, 1995
Flavobacterium sp.	Potato	De Boer and Copeman, 1974
	Rice	Elbeltagy *et al.*, 2000
Vibrio sp.	Corn	Fischer *et al.*, 1992
Gluconacetobacter sp.	Wheat	Luna *et al.*, 2010 Riggs *et al.*, 2001
	Sorghum	
	Maize	
	Rice	Meneses *et al.*, 2017
		Rouws *et al.*, 2010
	Sugarcane	Rouws *et al.*, 2010
Erwinia sp.	Sugar beet	Jacobs *et al.*, 1985
	Cotton	Misaghi and Donndelinger, 1990
	Alfalfa	Gagne *et al.*, 1987
Stenotrophomonas sp.	Cucumber	Mahaffee and Kloepper, 1997
Curtobacterium sp.	Maize	Liu *et al.*, 2012
	Red clover	Sturz *et al.*, 1998
	Soybean, Strawberry	Pereira *et al.*, 2012
	Vitis sp., Potato, Red clover	Collins *et al.*, 2004
	Grapevine	Bell *et al.*, 1995

	Rambutan	Suhandono *et al*., 2016
	Citrus	Araujo *et al*., 2001
Clavibacter sp.	Grapevine	Bell *et al*., 1995
	Cotton	Misaghi and Donndelinger, 1990
Streptomyces sp.	Jojoba	Elvia *et al*., 2017
Arthrobacter sp.	Red clover	Sturz *et al*., 1998
	Cucumber	Mahaffee and Kloepper, 1997
	Cotton	McInroy and Kloepper, 1995
Rhodococcus sp.	Jojoba	Elvia *et al*., 2017
Acidovorax sp.	Red clover	Sturz *et al*., 1998
Oceanobacillus sp.	Jojoba	Elvia *et al*., 2017
Burkholderia sp.	Citrus	Araujo *et al*., 2001
	Cucumber	Mahaffee and Kloepper, 1997
	Rice	Govindarajan *et al*., 2008
		Bacilo-Jimenez *et al*., 2001
	Cotton	Misaghi and Donndelinger, 1990
	Maize	Riggs *et al*., 2001
		Naveed *et al*., 2014
	Grapevine	Compant *et al*., 2005
		Compant *et al*., 2008
	Switchgrass	Kim *et al*., 2012
	Maize	Kost *et al*., 2014
	Wheat	Tian *et al*., 2017
	Sugarcane	Govindarajan *et al*., 2008
	Corn	McInroy and Kloepper, 1985
Methylobacterium sp.	Jojoba	Elvia *et al*., 2017
	Red clover	Sturz *et al*., 1998
	Citrus	Araujo *et al*., 2001
	Rice	Elbeltagy *et al*., 2000
Pseudomonas sp.	Strawberry	Tanpraset and Reed, 1997
	Cucumber	Mahaffee and Kloepper, 1997
	Red clover	Sturz *et al*., 1998

	Sugar beet	Jacobs *et al*., 1985
	Rough lemon	Gardner *et al*., 1982
	Grapevine	Bell *et al*., 1995
	Rice	Stolzfus *et al*., 1997
	Cotton	McInroy and Kloepper, 1995
	Alfalfa	Gagne *et al*., 1987
	Corn	Lalande *et al*., 1989
		Fisher *et al*., 1992
Herbaspirillum sp.	Sugarcane	Dong *et al*., 1994
	Rice	Reinhold-Hurek and Hurek, 1997 and 1998
		James *et al*., 2002
		Roncata-Maccari *et al*., 2003
		Elbeltagy *et al*., 2000
	Maize	Balsanelli *et al*., 2014
		Riggs *et al*., 2001
		Amaral *et al*., 2014
		Roncata-Maccari *et al*., 2003
		Brusamarello-Santos *et al*., 2017
	Wheat	Pankievicz *et al*., 2016
		Roncata-Maccari *et al*., 2003
	Sorghum	Roncata-Maccari *et al*., 2003
Sphingomonas sp.	Rice	Elbeltagy *et al*., 2000
Variovorax sp.	Red clover	Sturz *et al*., 1998
	Cotton	McInroy and Kloepper, 1995
Serratia sp.	Rough lemon	Gardner *et al*., 1982
	Red clover	Sturz *et al*., 1998
	Cotton	Misaghi and Donndelinger, 1990
Alcaligenes sp.	Citrus	Araujo *et al*., 2001
Rhodopseudomonas sp.	Rice	Elbeltagy *et al*., 2000
Acetobacter sp.	Sugarcane	Dong *et al*., 1994
Acinetobacter sp.	Cotton	McInroy and Kloepper, 1995

	Wheat	Patel *et al*., 2017
Xanthomonas sp.	Strawberry	Tanpraset and Reed, 1997
	Red clover	Sturz *et al*., 1998
	Grapevine	Bell *et al*., 1994
	Sugar beet	Jacobs *et al*., 1985
	Rough lemon	Gardner *et al*., 1982
	Cotton	Misaghi and Donndelinger, 1990
Cytophagales sp.	Rice	Elbeltagy *et al*., 2000
Pantoea sp.	Red clover	Sturz *et al*., 1998
	Citrus	Araujo *et al*., 2001
	Grapevine	Bell *et al*., 1994
	Rice	Elbeltagy *et al*., 2000
Enterobacter sp.	Red clover	Sturz *et al*., 1998
	Grapevine	Bell *et al*., 1994
	Cucumber	Mahaffee and Kloepper, 1997
	Rough lemon	Gardner *et al*., 1982
	Strawberry	Tanpraset and Reed 1997
	Cotton	McInroy and Kloepper, 1995
		Musson *et al*., 1995
	Corn	Fisher *et al*., 1992
		McInroy and Kloepper, 1985
	Maize	Naveed *et al*.,2014
		Riggs *et al*., 2001
	Wheat	Tian *et al*., 2017
Micrococcus sp.	Red clover	Sturz *et al*.,1998
	Potato	De Boer and Copeman, 1974
	Canola and wheat	Germida *et al*., 1998
Achromobacter sp.	Wheat	Patel *et al*., 2017
Rhizobium sp.	Red clover	Sturz *et al*., 1998
	Cotton	McInroy and Kloepper, 1995
Azorhizobium sp.	Rice	Stolzfus *et al*., 1997

		Reddy *et al.*, 1997
		Elbeltagy *et al.*, 2000
	Wheat	Webster *et al.*, 1997
Rathayibacter sp.	Canola and wheat	Germida *et al.*,1998
Azocarus sp.	Rice	Reinhold-Hurek and Hurek, 1997 and 1998
Rhodococcus sp.	Grapevine	Bell *et al.*, 1995

2.2 Phenotypic and genotypic identification of bacteria

The phenotypic and genotypic studies are required to identify and characterize the microbial strain (Donelli *et al.*, 2013). Phenotypically, bacteria are classified on specific criteria like colony morphology, cell morphology (Gram's reaction, motility), endospore staining, catalase test, gas, and ammonia formation (Holt *et al.*, 1994). In addition, the physiology of bacteria, such as growth rate at a different temperature, pH, and salt tolerance, were analyzed for proper identification (Tamang *et al.*, 2007). Furthermore, the biochemical tests are one of the inevitable studies for the preliminary classification and identification of bacteria. The tests includes sugar fermentation tests, IMViC (Indole Methyl red Voges-Proskauer Citrate) test, nitrate reduction, oxidase, and urease (Hammes and Hertel, 2003).

Genotypic microbial identification is based on profiling the genetic material (primarily DNA) of an organism. Genotypic methods are independent of the organism's growth phase and physiological conditions, thus owning phenotypic techniques. They are classified into two major types, sequence-based techniques and fingerprint or pattern-based techniques. Sequence-based methods traditionally analyze 16S rRNA gene sequence, which draws attention in establishing phylogenetic relationships among bacteria up to genus level classification. In contrast, fingerprinting-based methods are less reliable in phylogenetic comparison (Vandamme *et al.*, 1996). Also, the sequence-based techniques when coupled with phenotypic analysis can create a standard polyphase in finding new species of bacteria (Gillis *et al.*, 2001).

Pattern-based techniques typically use a systematic method to produce an array of fragments from the chromosomal DNA of an organism. These fragments generate a unique profile or fingerprint of the organism and its closely related species. Thus, researchers can develop a database of fingerprints from known organisms to test and compare the unknown strains (Emerson *et al.*, 2008). Presently, fingerprinting techniques such as repetitive element PCR (rep-PCR), amplified fragment length polymorphism (AFLP), and random amplification of polymorphic DNA are designed to take advantage of DNA polymorphisms in closely related organisms that has occurred due to various evolutionary mechanisms (Settanni and Corsetti, 2007). This technique incorporates PCR to amplify short segments of DNA into multiple copies using appropriate primers (Versalovic *et al.*, 1994, Cocconcelli *et al.*, 1995). Bioinformatics is the principal tool, which contributes to searching sequence similarity with and within genetic sequences. BLAST is the most widely used tool in bioinformatics (Lin *et al.*, 1996).

Table no. 2.2 Commonly used primers targeting bacterial 16S rRNA gene sequence.

Primers	Sequence 5’- 3’	References
8F 1492R	AGAGTTTGATCMTGGCTCAG GGYTACCTTGTTACGACTT	Lane (1991)
8F(a) 1391R	AGAGTTTGATCCTGGCTCAG GACGGGCGGTGWGTRCA	Lane (1991); Ley *et al.*, (2006)
27F 1492R	AGAGTTTGATCCTGGCTCAG TACCTTGTTACGACT	Dojka *et al.*, (1998)

BAC338 BAC805R	ACTCCTACGGGAGGCAG GACTACCAGGGTATCTAATCC	Yu *et al.*, (2005)
341Fb 907R	CCTACGGGAGGCAGCAG CCGTCAATTCMTTTGAGTTT	Muyzer *et al.*, (1993) Muyzer and Smalla (1998)
341F 534R	ACTCCTACGGGAGGCAGCAG ATTACCGCGGCTGCTGG	Garcia-Bernet *et al.*, (2011)
27F 518R	GAGTTTGATCMTGGCTCAG WTTACCGCGGCTGCTGG	Lagier *et al.*, (2015)
27F 338R	AGAGTTTGATCMTGGCTCAG GCTGCCTCCCGTAGGAGT	Suzuki and Giovannoni (1996)
784F 1061R	AGGATTAGATACCCTGGTA CRRCACGAGCTGACGAC	Andersson *et al.*, (2008)

Conventional nucleic acid codes are used with M=A or C, Y=T or C, R=A or G, and W=A or T.

2.3 Bacterial community analysis using NGS technology

Metagenomics study efficiently displays genomic information of individual taxa of uncultured endophytic microbial communities (Dinsdale *et al.*, 2008). Sessitsch *et al.*, (2012) investigated putative functions deduced from protein-coding gene fragments of endophytic bacterial colonization in rice roots. This helps to predict characters or prominent features like plant-polymer degrading enzymes, protein secretion systems, quorum sensing, detoxification of free radicals, etc., and metabolic processes playing a pivotal role in endophytic lifestyle.

Monteiro *et al.*, (2012) applied metagenomics to study the colonization pattern from the genes of two closely related species, endophytic *Herbaspirillum seropedicae* SmR1, showing no disease symptoms and the phytopathogenic *H. rubrisubalbicans* M1, causing mottled stripe disease. The result shows differences in the colonization patterns on constructing the suppression subtractive hybridization (SSH) libraries. In 2015, Akinsanya *et al.*, applied the high throughput sequencing techniques to study endophytic bacterial communities in *the Aloe vera* plant by evaluating its PCR amplicon of 16S rDNA sequences (V3–V4 regions). The analysis reports that the roots have the most extensive composition when compared to stems and leaves. Guo *et al.*, (2015) applied this technique in wild and cultivated species of *Zizania latifolia*, which revealed continuous long-standing colonization of endophytes has significant effects on the structural and transcriptomic components of the host plant genome. Furthermore, Zgadzaj *et al.*, (2015), in their study on *Lotus japonicus*, reported that the host genome implies a significant role in determining a wide range of taxa of endophytic bacteria and the symbiont taxa within root-nodules. Therefore, the study specifies that the host genetic factors control the diversity of microbes associated with the host plant.

Tian *et al.*, (2015) investigated the root microbiome by infected tomatoes with root-knot nematodes. They observed the effects and response of the bacterial endophytes before and after nematode attacks to unveil the functional attributes of microbes. Their data indicated the previously assumed bacterial associates with nematode might be responsible for nematode infections of the tomato roots. Yang *et al.*, (2015) performed a 16S rDNA analysis from the samples collected from five sites of the noni plant (roots, branches, leaves, fruits, and seeds). The results depict that these five parts harbor a similar bacterial composition with the *Sphingomonas*, *Pseudomonas*, *Halomonas*, and *Geobacillus*. Utturkar *et al.*, (2016) described the enrichment and separation of endophytic bacteria from *Populus* roots using modified differential and density gradient centrifugation-based methods.

The diversity of the endophytic bacterial community in the root of rice (*Oryza sativa* L.) was studied by Sengupta *et al*., (2017) reports that the *Bacillus* is the most dominant endophytic genera in rice roots, which helps in nitrogen fixation. Using 454 pyrosequencing platforms, Tanjung *et al*., (2017), studied endophytic bacteria from oil palm fruits that identified annotated contigs sequences of eight bacterial species based on abundance. Through NGS technology, Khan *et al*., (2017) analysed the rhizospheric bacterial and fungal diversity of the cultivated and wild *Boswellia sacra* tree populations that points out higher glucosidases, cellulases and indole-3-acetic acid were found in cultivated tree population in comparison with wild tree type. Moreover, applying Illumina-based analysis, Yang *et al*., (2017) effectively captured endophytic bacterial diversity of tree peony in roots and leaves in their work. Their findings profiled that both the tissues and plant genome are involved in shaping the endophytic bacterial communities.

A high-throughput sequencing approach for monitoring 16S rRNA variability was studied by Medo *et al*., (2018), reports the changes in endophytic bacterial diversity due to mutagenic effects in selected M1-M15 generations in the varieties Ficha and Pribina of *Amaranthus cruentus*. The findings shows that after gamma radiation, the metagenomic libraries of Ficha and Pribina have different profiles of identified bacteria in M1 and M7 generations. Using this technology, Mareque *et al*., (2018) evaluated the use of nitrogen fertilizer in field-grown sweet sorghum in affecting the endophytic and diazotrophic bacterial community's structure and diversity abundance composition**.**

Santhosh and Anto (2020) reported the dominance of genus *Brevundimonas*, *Bacteroides* followed by *Serratia* and *Propionibacterium* in the community study of endophytic bacteria prevailing in the leaves of *Morinda pubescens*. Xia *et al*., (2020) by high-throughput sequencing 16S rDNA analyzed the endophytic bacterial diversity and functional genes in the rose plant that involved in the metabolism of carbohydrates and amino acids, cellular processes, and signalling.

2.4 Beneficial aspects of bacteria

2.4.1 Bioactive compounds from bacteria

Most microbes, such as bacteria, fungi, actinomycetes, microalgae, etc., produce innumerable bioactive compounds. For large-scale production of these compounds, isolates require different environmental conditions and primary metabolites like carbon, nitrogen sources (Shukla, 2015). Microbially-derived compounds contributes host physiological and pathological conditions such as controlling cardiovascular diseases, cholesterol anabolism, obesity, and metabolic syndrome. Lactic Acid Bacteria (LAB) can develop bioactive amino acids and peptides that ensure antioxidant and immunomodulatory effects. Also, these bacteria control hyperglycemia, hypercholesterolemia, hypertension, cell cycle regulation, and apoptosis (Mazzoli *et al*., 2017).

Streptococcus sp. and *Fusobacterium* sp. are tannin-degrading bacteria that can generate gallic acid and pyrogallol. These secondary metabolites act as an anti-carcinogen. Also studies reported that microbial-derived amines could modulate a set of physiological functions such as allergy, muscle relaxation, anxiety, digestion, depression (Pessione *et al*., 2005). LAB organisms are a significant repository of gamma-aminobutyric acid (GABA) contributing to neurons, endocrine, and immune cells (Laroute *et al*., 2016). Most of the microbially-derived compounds show antagonistic activity against various plant and human pathogens. In addition to this, some microbial secondary metabolites or compounds show antioxidant, anti-inflammatory, cytotoxic, anticancer, and other biological activities. Some of the bacterial bioactive compounds are listed below.

Table no. 2.3 Some selected bioactive compounds reported from bacteria.

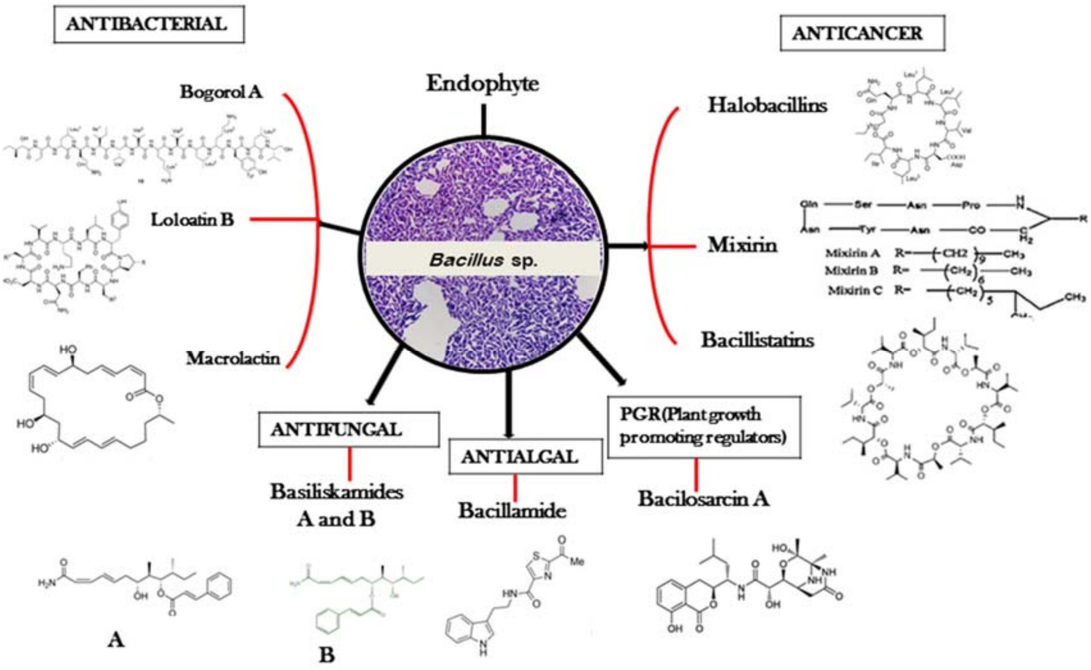
Bioactive compound	Source	Activity	References
Bacteriocins	*Lactococcus lactis*	Antimicrobial	Sturme *et al.*, (2002); Sankar *et al.*, (2012)
Tauramamide, ethyl esters	*Brevibacillus laterosporus*	Antimicrobial	Desjardine *et al.*, (2007)
Lipoxazolidinone A, B and C	*Marinispora* sp.	Antimicrobial	Macherla *et al.*, (2007)
Lynamicins A and B	*Marinispora* sp	Antimicrobial	McArthur *et al.*, (2008)
Zafrin	*Pseudomonas stutzeri*	Antimicrobial	Uzair *et al.*, (2008)
Ayamycin	*Nocardia* sp.	Antimicrobial	El-Gendy *et al.*, (2008a)
Streptomycin	*Streptomyces griseus*	Antimicrobial	Waksman *et al.*, (1946)
Enterocins	*Enterococcus casseliflavus*	Antimicrobial	Indira *et al.*, (2018)
Fijimycins A-C and etamycin A	*Streptomyces* sp.	Antimicrobial	Peng *et al.*, (2011)
Heronamycin A	*Streptomyces* sp. (MB-M-0392)	Antimicrobial	Raju *et al.*, (2012)
Halolitoralin A , B and C	*Halobacillus litoralis* YS3106	Antimicrobial	Ling *et al.*, (2002)
1-acetyl-beta-carboline	*Pseudomonas* sp. UJ-6	Antimicrobial	Lee *et al.*, (2013)
Essramycin	*Streptomyces* sp. Merv8102	Antimicrobial	El-Gendy *et al.*, (2008b)

Macrolactin W	*Bacillus* sp. 091D194	Antimicrobial	Mondol *et al*., (2011)
Cyclic tetrapeptides	*Pseudomonas* sp.	Antimicrobial	Rungprom *et al*., (2008)
2, 2’, 3-Tribromo-phenyl 4, 4'-dicarboxylic acid	*Pseudoalteromonas* sp.	Antimicrobial	Alim *et al*., (2009)
Urdamycinone E, urdamycinone G and Dehydroxyaquayamycin	*Streptomyces* sp. BCC 45596	Antimicrobial	Supong *et al*., (2012)
Bogorol A	*Bacillus* sp.	Antimicrobial	Barsby *et al*.,(2001)
Loloatin B	*Bacillus* sp. PNG276	Antimicrobial	Gerard *et al*.,(1996)
Ariakemicins A and B	*Rapidithrix* sp.	Antimicrobial	Oku *et al*., (2008)
Macrolactin S and V	*Bacillus amyloliquefaciens*	Antimicrobial	Gao *et al*., (2010)
Basiliskamides A and B	*Bacillus laterosporus*	Antimicrobial	Barsby *et al*., (2002)
Cycloheximide	*Bacillus amyloliquefaciens*	Antimicrobial	Liu *et al*., (2018)
Lipopeptides	*Bacillus subtilis*	Antimicrobial	Gond *et al*., (2015)
Polyketide synthase	*Brevibacterium* sp.	Antimicrobial	Wei *et al*., (2018)
Fusaricidin A-D	*Paenibacillus polymyxa*	Antimicrobial	Beck *et al*., (2003)
Xiamycin	*Streptomyces* sp.	Antiviral	Ding *et al*., (2010)
Indosespene, Sespenine	*Streptomyces* sp.	Antimicrobial	Ding *et al*., (2011)
Maytansine	*Streptomyces* sp.	Antimicrobial Anticancer	Zhao *et al*., (2005)
Munumbicins, munumbicin D	*Streptomyces* sp.	Antimicrobial	Castillo *et al*., (2002)
Biphenyls	*Streptomyces* sp.	Antimicrobial	Taechowisan *et al*.,

		Anticancer	(2017)
Decursin	*Streptomyces* sp.	Antimicrobial	Taechowisan *et al*., (2013)
Alnumycin	*Streptomyces* sp.	Antimicrobial Anticancer	Bieber *et al*., (1998)
p-Aminoaceto-phenolic acids	*Streptomyces griseus*	Antimicrobial	Guan *et al*., (2005)
Actinomycins D	*Streptomyces parvulus*	Antimicrobial	Chandrakar and Gupta, (2019)
Lantibiotics	*Bacillus subtilis*	Antimicrobial	Deng *et al*., (2011)
Surfactin, fengycin, and iturin A	*Bacillus subtilis*	Antimicrobial	Cazorla *et al*., (2007)
NRPS and trans-acyl transferase PKS1	*Bacillus velezensis*	Antimicrobial	Cai *et al*., (2017)
Lactic acid	*Lactobacillus* sp.	Chlolestrol metabolism	Tachedjian *et al*.,(2017); LeBlanc *et al*., (2017)
Butyric acid	*Faecalibacterium* sp. *Butyricicoccus* sp. *Roseburia* sp.	Anti-inflammatory and antitumor	Geirnaert *et al*., (2017); Miremadi and Shah, (2012)
Propionic acid	*Propionibacterium* sp.	Gluconeogensis	Vorobjeva *et al*., (2008)
Acetic acid	*Bifidobacterium* sp.	Defense functions	Fukuda *et al*., (2012)
Inulins and levans	*Lactobacillus gasseri*	Reduces fat and cholesterol absorption	Anwar *et al*., (2010)
Riboflavin	*Lactococcus lactis*	Energy metabolism	Cardenas *et al*., (2015)
Pyridoxine	*Bifidobacterium sp.*	Aminoacid metabolism	Patel *et al*., (2013)
Amylase	*Lactobacillus sp.*	Starch hydrolysis	Padmavathi *et al*., (2018)
Halobacillin	*Bacillus* sp. CND-914	Anticancer	Trischman *et al*., (1994)
Mixirin	*Bacillus* sp.	Anticancer	Zhang *et al*., (2004)

Marinopyrroles A and B	*Streptomyces sannurensis*	Cytotoxic	Hughes *et al*., (2008)
Bacillistatins	*Bacillus silvestris*	Anticancer	Pettit *et al*., (2009)
Coronamycins	*Streptomyces* sp.	Antibiotics	Ezra *et al*., (2004)
Kakadumycins	*Streptomyces* sp.	Antibiotics	Castillo *et al*., (2003)
Exopolysaccharides	*Bacillus amyloliquefaciens*	Anticancer	Chen *et al*., (2013)
Polysaccharides	*Bacillus thuringiensis*	Anticancer	Ramamoorthy *et al*., (2018)
Lupinacidins A and B	*Micromonospora lupini*	Anticancer	Igarashi *et al*., (2006)
Maytansine	*Streptomyces* sp.	Anticancer	Lu and Shen (2003)
4-Arylcoumarins	*Streptomyces aureofaciens*	Anticancer	Taechowisan *et al*., (2007)
Bafilomycin D	*Streptomyces cavourensis*	Anticancer	Vu *et al*., (2018)
Pterocidin	*Streptomyces hygroscopicus*	Anticancer	Igarashi *et al*., (2007)
Salaceyins A and B	*Streptomyces laceyi*	Anticancer	Kim *et al*., (2006)
Spoxazomicins A-C	*Streptosporangium oxazolinicum*	Anti-trypanosomal	Inahashi *et al*., (2011a,b)
Auxins, Siderophores	*Bacillus sp.*	Plant growth promoter and seed germination	Sabate *et al*., (2018)
Indole acetic acid, potassium and zinc solubilisation	*Bacillus amyloliquefaciens*, *Bacillus cereus* and *Bacillus subtilis*	Plant growth promoter	Pena-Yam *et al*., (2016); Gowtham *et al*., (2018)
Bacilosarcin A	*Bacillus subtilis*	Plant growth regulator	Azumi *et al*., (2008)

Fig. 2.1 Schematic representation of bioactive compounds produced by *Bacillus* sp.



2.4.2 Bacteria in Nanotechnology

Nanotechnology is an integral part of the biotechnology used for gene delivery and cell labeling in plants and medicine. It can also apply as a sensor in research in agriculture for detecting many biomolecules (Wang *et al*., 2006). Husseiny *et al*., (2007) investigated the bacterial strain *Pseudomonas aeruginosa* ATCC 90271 has potentiality for extracellular biosynthesis of gold nanoparticles, and TEM micrograph shows well-dispersed AuNps. Marine bacteria are explored for gold nanoparticles (AuNPs) production. In 2007, Prasad *et al*., synthesized and characterized titanium nanoparticles by an eco-friendly approach using *Lactobacillus* sp. The XRD and TEM results shows that titanium nanoparticles were spherical with a size of below 60 nm.

In 2012, Sharma *et al*., identified a novel strain, *Marinobacter pelagius*, which can synthesize stable, monodisperse, polyphasic gold nanoparticles. Thomas Roshmi *et al*., (2012) explored the nanoparticle synthesizing property of an endophytic bacterium *Bordetella* sp. isolated from *Piper nigrum*. Additionally, Thomas *et al*., (2012) focussed on utilizing the nanoparticle synthesized from novel marine bacteria *Pseudomonas* strain for their antibacterial efficacy against *Salmonella typhi*, *Vibrio cholerae*, *Bacillus subtilis*, and *Staphylococcus aureus*. In another work, Thomas *et al*., (2014) successfully demonstrated an attempt of synthesizing biogenic silver nanoparticles from marine bacterial isolate, *Ochrobactrum anthropi*, and its application on pathogenic bacteria proves good antagonistic activity. Das *et al*., (2014) reported the synthesis and characterization of silver nanoparticles by a bacterial strain (CS 11) from heavy metal contaminated soil. Also, Anthony *et al*., (2014) studied silver nanoparticles production efficacy of a novel strain, *Bacillus marisflavi* isolated from agricultural wastes.

Furthermore, Roshmi *et al*., (2015) reported the synthesis of highly stable AuNPs from soil *Bacillus* sp., which act as an effective drug delivery vehicle against multidrug-resistant bacteria. Even though AuNPs have no antibacterial activity, they showed very effective activity against Coagulase-negative staphylococcus (CoNS) strains compared to pure drugs. Finally, Roshmi *et al*., (2016) reported the photocatalytic degradation of methylene blue by silver nanoparticles synthesized by *Bacillus subtilis* SJ 15; in addition, nanoparticles showed excellent antimicrobial properties.

The study conducted by Singh *et al*., (2018) found that microorganisms secrete enzymes and biological molecules that detoxify metal ions to less toxic metal nanoparticles by reducing metal ions responding to environmental stress. In addition, El-Gamal *et al*., (2018) reported that rare actinobacteria could synthesize nanoparticles. Likewise, Hassan *et al*., (2019) investigated the isolation and utilization of endophytic *Streptomyces zaomyceticus* Oc-5 and *Streptomyces capillispiralis* Ca-1 from the plant *Oxalis corniculata* and *Convolvulus arvensis*, respectively, for the nanoparticles biosynthesis. In 2019, Ibrahim *et al*., in their work pointed out the synthesized AgNPs from endophytic bacterium *Bacillus siamensis* strain C1 isolated from the plant *Coriandrum sativum*, shows AgNPs significant inhibition on bacterial growth and biofilm formation. Along with this, AgNPs were found to protect rice plants from bacterial infection and promote plant growth.

In 2020, Ahmed *et al*., in their studies, targeted biogenic silver nanoparticles (AgNPs) natively synthesized by *Bacillus cereus* strain SZT1 to control Bacterial Leaf Blight (BLB) by significantly increasing the plant biomass and antioxidant enzyme activity along with decreasing the cellular concentration of free radicals. The extracellular production of IONPs nanoparticles from *Proteus vulgaris* ATCC-29905 was reported by Majeed *et al*., (2020). The studies show that IONPs synthesized were cytotoxic against U87 MG-glioblastoma cancer cells and inhibit cell migration of HT-29 cancer cells. In addition, IONPs exhibit potential antioxidant and antibacterial activity. Furthermore, Jubran *et al*., (2020) studied *Bacillus* sp. with an eco-friendly approach capable of producing Fe_3O_4 nanoparticles at pH, temperature, and incubation time.

2.4.3 Antimicrobial activity of bacteria

The genus *Streptomyces* showed the most antimicrobial activities among all isolated actinomycetes. Zheng *et al*., (2000) screened the actinomycetes having antitumor and antimicrobial activity from the surface epidermis of sea plants and animals collected from the Taiwan Strait of China. The antimicrobial study of endophytic bacterial isolate *Bacillus amyloliquefaciens* UD25 by Bhoonobtong *et al*.,

(2012) evaluated that the diethyl ether and chloroform extract of the isolate shows bacteriostatic activity against *Staphylococcus aureus*. Fitriani *et al*., (2015) isolated endophytic bacterial strains *Shewanella* sp. and *Pseudomonas* sp. from roots of *Ageratum conyzoides* and was screened for the antibacterial activity with the crude extract of endophytic bacterial supernatant. The study indicates that *Shewanella* sp. shows the highest level inhibition zone against *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*.

Sabu and Radhakrishnan (2016) isolated five strains of endophytic bacteria *Bacillus* from the rhizome of *Zingiber officinale*. These strains were screened for the antibacterial potentiality against human pathogenic bacteria. In addition, broad-spectrum antibacterial properties of an another endophytic *Bacillus* species, *Bacillus mojavensis*, were analyzed by Jasim *et al*., 2016. Further studies that relied on LC-MS/ MS proved the organism's ability to produce lipopeptides surfactin and fengycin. Shinta *et al*., (2016) analyzed the antibacterial activity of the compound Nonanoic acid ethyl ester from *Pseudomonas aeruginosa* strain SV1 isolated from *Ficus variegata.* The antibacterial compound was found effective against pathogenic bacteria like *Staphylococcus aureus*, *Bacillus subtillis*, *Escherichia coli*, and *Pseudomonas aeruginosa*.

Phenotypically varied bacterial endophytes isolated from the segments of *Ophioglossum reticulatum* by Mukherjee *et al*., (2017) were assayed for antimicrobial properties by cross-streak and agar-cup assay methods. The results show antibiotic production by the potent endophytic bacterial isolate OPL 19 identified as *Bacillus safensis* in tryptic soy broth. In 2017, Beiranvand *et al*., in their studies, screened twenty-three medicinal plant samples of Iran for endophytic bacterial isolate having potent antibiotic compound. Sixteen out of twenty-three bacterial isolates (69%) exhibited antimicrobial activity against the selected human pathogenic bacteria.

The antifungal activity of endophytic bacterial strains of *Bacillus* sps. from the leaves of *Morinda citrifolia* L. against *Fusarium oxysporum* was carried out by Agustien *et al*., (2017). Mohamad *et al*., (2018) reported sixteen endophytic strains from *Glycyrrhiza uralensis* having antimicrobial activities against various fungal pathogens. Among the isolated strains, *Bacillus atrophaeus* and *Bacillus mojavensis*, containing putative gene encoding polyketide synthase, non-ribosomal peptide synthetase, and lytic enzymes have broad antimicrobial activity. Nxumalo *et al*., (2020), in their study, isolated and screened thirteen endophytic bacterial strains from the leaves of *Anredera cordifolia* CIX1 for the biologically active metabolites showing the antibacterial and antioxidant through GC-MS analysis, which revealed fifteen active compounds.

2.4.4 Antioxidants property of bacteria

Oxidative stress is an imbalance of prooxidant and antioxidants in the cell, resulting in lipid peroxidation, protein denaturation, DNA hydroxylation, and apoptosis. Probiotics consumption meets the requirement of antioxidants in the human diet to reduce oxidative cell damage. Lactic acid bacteria isolated from various environmental sources are excellent antioxidants. The antioxidant activity of probiotics strains belonging to genus *Lactobacillus*, *Bifidobacterium,* and *Propionibacterium* was investigated by Afify *et al*., (2012) through the 1,1-diphenyl -2-picrylhydrazyl radical (DPPH) and 2,2’-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) scavenging in comparison with standards ascorbic acid and Butylated hydroxytoluene (BHT), respectively. The results showed maximum antioxidant activity with *Propionibacterium freudenreichii* and *Lactobacillus retueria*. Moreover, Abubakr *et al*., (2012) isolated the whey produced by seven isolates of lactic acid bacteria (LAB) due to the proteolytic activity on skim milk agar from different food samples. The isolates after three days of fermentation were found to have free radical scavenging potency. Saduakhasova *et al*., (2013) observed a significantly high level of the total antioxidant activity of the probiotic consortium intact cell. DNA-protective action, and. The total antioxidant activity of probiotic bacteria consortia was determined. Amaretti *et al.,* (2013) isolated thirty-four strains of lactic acid bacteria that have in vitro antioxidant activity against ascorbic and linolenic acid oxidation. The genera include *Bifidobacterium*, *Lactobacillus*, *Lactococcus*, and *Streptococcus*.

Balraj *et al*., (2014) reported 19 varied pigmented marine bacterial strains belonging to genus *Exiguobacterium* sp. isolated from water samples collected from Chennai, Rameshwaram, Tuticorin, and Cochin, India. Out of nineteen isolates, extracted pigments of one isolate showed antioxidant activity against 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical. Selim *et al*., (2015) examined DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging activity of crude exopolysaccharides of eighty-three isolates from marine (the Mediterranean and Red Seas) and soil habitats. The result displayed nine isolates belonging to the genus *Bacillus* has potent antioxidant property

The antioxidant property of endophytic bacteria *Lactobacillus* sp. isolated from the leaves of *Adhathoda beddomei* was analyzed by Swarnalatha *et al*., (2015) analysed ethyl acetate extract for DPPH activity and the qualitative analysis indicated high levels of phenolic compounds. Next, Nyanzi *et al*., (2015) investigated the antibacterial and antioxidant properties of methanol extracts of freeze-dried cells of probiotic *Lactobacillus* strains which showed effective DPPH scavenging activity. Finally, Fessard *et al*., (2016) studied the antioxidant capacity of ten LAB from six samples of tropically grown fruits and leaves. In particular, studies reported two isolates, S14 (*Leuconostoc pseudomesenteroides*) and S27 (*Weissella cibaria*), showed increased antioxidant capacity in pineapple juice to alleviate nutritional food quality. In addition the highly variable tolerance capacity of isolates towards acid, oxidative, or salt stress were noted.

Using YEMA agar medium, Radhakrishnan *et al*., (2016) extracted crude pigment from the *Streptomyces* sp. D25 using ethyl acetate for antioxidant study in DPPH and nitric acid scavenging assay, respectively. Wang *et al*., (2017) reviewed the mechanisms and mode of probiotics to improvise the antioxidant system and their ability to scavenge the free radical generation. In addition, reviews on the study conducted in recent years explain oxidative stress is highly associated with distorted gut microbiota.

2.4.5 Anti-inflammatory activity of bacteria

The anti-adhesive and anti-chemotactic entity of *Staphylococcus aureus* involves leukocytes' homing mechanism with anti-inflammatory activity was reported by Chavakis *et al*., (2007) in their work. Rostami *et al*., (2016) performed biological studies such as antimicrobial, antioxidant, anticancer, and anti-inflammatory using carotenoid pigments isolated from *Micrococcus roseus* and *Rhodotorula glutinis* that indicates both the pigments extracted from the bacteria inhibited the 12-*O*-tetradecanoylphorbol-13-acetate (TPA) induced inflammation. Research on the anti-inflammatory activity of methanol extract and fractions of bacteria associated with the sponge (*Haliclona amboinensis*) was performed by Andriani *et al*., (2017). The study highlighted their effect in decreasing nitric oxide (NO) production more significantly than 80% and inhibiting cyclooxygenase-1 (COX-1), cyclooxygenase-2 (COX-2), and secretory phospholipase A2 (sPLA2) activity.

The investigation of Paynich *et al*., (2017) using exopolysaccharide (EPS) from probiotic spore-forming bacterium *Bacillus subtilis* to study the anti-inflammatory activity was done using M2 Macrophages to inhibit T Cell-Mediated Disease. EPS from the probiotic bacterium protects mice from acute colitis caused by *Citrobacter rodentium*. Furthermore, results show that the in-vitro inhibition of CD4+ and CD8+ T cells activation by M2 macrophages and in vivo transfer of macrophage-rich peritoneal cells from EPS-treated donor mice to the recipient confirms protection against T cell-mediated diseases. The study on acute inflammation in mice using the bright yellow-pigmented bacterial isolate *Brevibacterium* sp. isolated from different sampling sites at the sea surface Visakhapatnam coastal areas (Srilekha *et al*., 2017) resulted an inhibition of cyclooxygenase-2 (COX) enzyme, thereby reducing paw edema in mice. Likewise, Srilekha *et al*., (2018) conducted the anti-inflammatory effect and in vivo wound healing activity in albino mice using the yellow pigments extracted from *Micrococcus* marine bacteria from seawater in different coastal areas Nellore. Ibrahim *et al*., (2018) investigated the anti-inflammatory activity of bioactive constituent (saphenic acid derivative of 1-phenazinecarboxylic acid) of marine isolate *Brevibacterium aureum* on induction of cytokines in lipopolysaccharide (LPS)-stimulated macrophages. The expression of pro-inflammatory (cytokines) mediators signaling pathway was analyzed by western blot technique. The result significantly pointed out the reduced level of expression in LPS-induced NF-κB and MAPKs phosphorylation.

Ibrahim *et al*., (2019) studied the invivo anti-inflammatory activity of exopolysaccharide (EPSBa3) fractions of *Bacillus axarquiensis* NRC G6 on the carrageenan-induced paw edema in mice. In addition, the finding supports the reduction in nitric oxide (NO), lipid peroxidation (LPO), reactive oxygen species (ROS), and interleukin-6 (IL-6) protein expression as a result of carrageenan-induced edema. From the methanol extract of *Exiguobacterium acetylicum,* Jinendiran *et al*., (2020) isolated six structurally different carotenoids for the evaluation of the biological activity. The findings revealed that all the six carotenoids blocked colorectal cancer (HT-29) in a dose-dependent manner and also inhibited LPS-induced NO production, tumor necrosis factor-alpha, and lipid peroxidation with great anti-inflammatory activity.

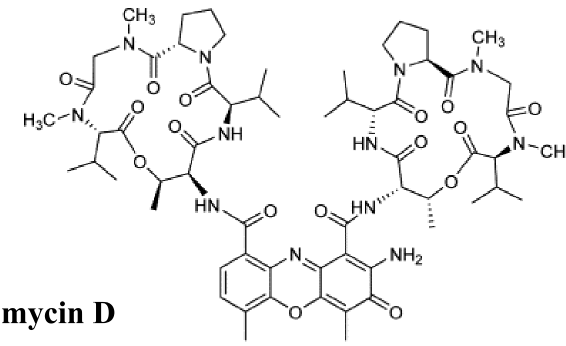
2.4.6 Bacteria in cancer therapy

Microbial drugs are making an unremitted influence on cancer therapy. The invention of actinomycin ventured into the microbial world in quest of anticancer drugs. The genus *Streptomyces* is considered as a storehouse of bioactive compounds. Also, some approved products draw special attention in cancer treatments. Actinomycins, anthracyclines, bleomycin, mitosanes, mithramycin, streptozotocin, pentostatin, enediynes, taxol, and epothilones are among those drugs (Mahajan *et al*., 2013).

2.4.6.1 Actinomycins

Actinomycin D (1) (dactinomycin), a member of the family Actinomycin group of compounds, was isolated from several strains of *Streptomyces* (Avendano and Menendez, 2015). Dactinomycin is used to treat sarcomas, pediatric solid tumors like Wilms' tumor (a type of renal tumor), testicular cancer, and choriocarcinoma (Gallego *et al*., 1997). Actinomycin K isolated from *Streptomyces melanochromogenes* was reported as an active compound against neoplasm was (Xu *et al*., 2012).

(1)

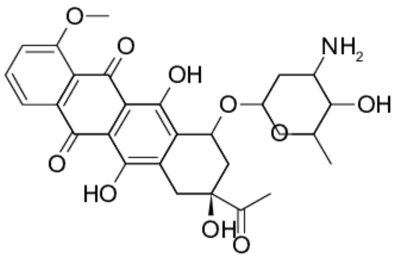


Actinomycin D

2.4.6.2 Anthracyclines

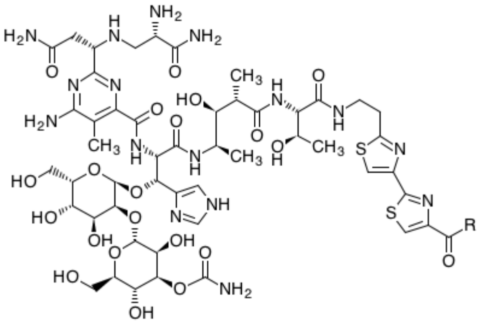
Anthracyclines are the most effective drug to treat cancer when compared to any other class of chemotherapeutic agents. The first discovered anthracycline was Daunomycin (2) (1996) which was naturally produced by *Streptomyces peucetius*. In addition, USFDA in 1973 approved bleomycin (3), a glycopeptide produced by *Streptomyces verticillus* (Umezawa *et al*., 1966).

(2)



Daunomycin

(3)

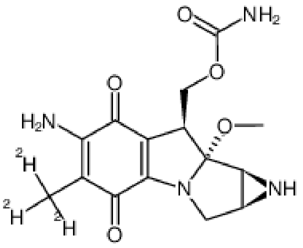


Bleomycin

2.4.6.3 Mitosanes

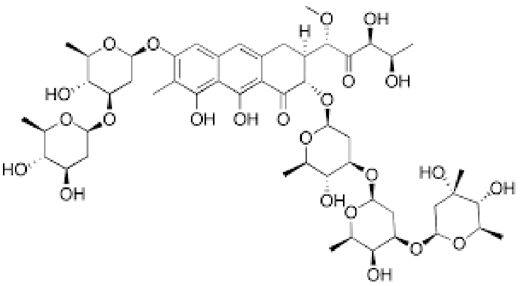
Mitosanes act as an excellent antitumor agent in treating a wide range of cancers. Food and Drug Administration (FDA) in 1974 approved Mitomycin C against lung, breast, bladder, anal, colorectal, head, and neck cancers, including melanomas and gastric or pancreatic neoplasms. Most of the mitomycin (4) is produced on the fermentation of the bacterium *Streptomyces caespitosus*. Mithramycin (5), an aromatic polyketide was developed from *Streptomyces argillaceous*. It is an antibacterial and antitumor drug used in treating testicular cancer, neoplasms, and hypocalcemia (Lombo *et al*., 1996).

(4)



Mitomycin C

(5)

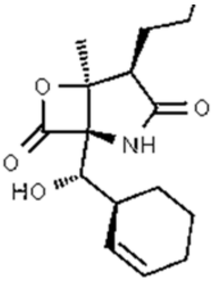


Mithramycin

2.4.6.4 Other bacterial anticancer drugs

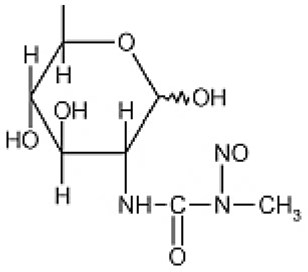
Salinosporamide A (6), a potent proteasome inhibitor isolated from marine actinomycetes, *Salinispora tropica,* is a novel anticancer drug for treating multiple myeloma (Gulder and Moore, 2010). Streptozotocin (7), isolated from *Streptomyces achromogenes*, is a microbial metabolite having antitumor properties (Abdollahi and Hosseini, 2014). FDA approved streptozotocin for the treatment of pancreatic islet cell cancer in 1982. Pentostatin (8), a purine analog developed by *Streptomyces antibioticus*, interferes with the cell's ability to process DNA (Aronson, 2016). Calicheamicin (9), potent antitumor metabolites produced by *Micromonospora echinospora*, shows antitumor activity by breaking double-stranded DNA (Kumar *et al.*, 2017).

(6)



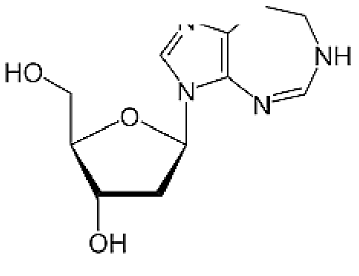
Salinosporamide A

(7)



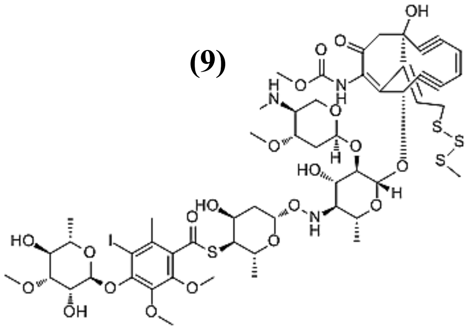
Streptozotocin

(8)



Pentostatin

(9)



Calicheamicin

Ohba *et al*., (2009) reported "Parasporin" heterogeneous cry proteins produced by *Bacillus thuringiensis* are found to have cytocidal activity for human cancer cells. A marine bacterium, *Bacillus subtilis*, produces eleven amicoumacins, including four novel lipoamicoumacins A-D, one new bacitracin C, and six known analogs with significant cytotoxic activity against HeLa cells (Li *et al*., 2012). The anticancer property of aqabamycin A-B (nitro maleimide) and aqabamycin E-G (Maleimide oxime) compounds isolated from *Vibrio anguillarum* was reported (Jalal *et al*., 1989; Imamura *et al*., 1994). In addition, the bacterial strain also produces antitumor agents like Pelagiomicin C (Phenazine) and Anguibactin (Catechol hydroxamate). Weber *et al*., (2004) isolated Brefeldine A compound from endophytic bacteria *Phoma medicaginis* having apoptosis activity in cancer cells.

The anticancer property of the marine bacteria was carried out by Ravuri and Kumari (2013) using the trypan blue exclusion method, which shows that these isolates produce secondary metabolites. The results showed that anticancer and apoptosis activity was maximum at a concentration of 100 µg against human breast cancer cell lines. Jeong *et al*., (2008) isolated 93 marine bacteria; out of it, *Bacillus vallismortis* exhibits the most potent cytotoxic activity on three colon cancer cells (HT-29, SW480, and HCT116). Finally, Maria Maruna *et al*., (2010) isolated a new strain *Streptomyces flavidofuscus* AC113 from *Taxus baccata* L. roots. The strain produced three major metabolites methyltetrangomycin, methyltetrangulol, and hydroxytetrangomycin.

2.4.7 Medicinal property of the plant *Morinda* L. species

2.4.7.1 *Morinda citrifolia* L.

The plant has excellent natural medicinal properties like antimicrobial, antioxidant, anti-inflammatory, and anticancer (Carrillo-Lopez and Yahia, 2011). The plant contains polysaccharides, amino acids, fatty acids, sterol, carotenoids, flavonoids, and anthraquinones (Chan-Blanco *et al*., 2006). An anthraquinone named Damnacanthal was reported in noni plants that target tyrosine kinases conferring antitumor activity (Garcia-Vilas *et al*., 2015). Noni has traditionally been reported for treating colds, flu, diabetes, anxiety, depression, and high blood pressure. Even though the scientific evidence concerning noni benefits is limited, some anecdotal evidence proves effective in treating colds and influenza. Noni fruits have been assessed as a substrate for probiotic juice by bacteria such as *Bifidobacterium longum*, *Lactobacillus plantarum*, and *Lactobacillus casei* (Wang *et al*., 2009).

2.4.7.2 *Morinda pubescens* J.E Smith

Various research on antioxidant, anti-inflammatory, cytotoxicity, and anticancer were reported in this plant (Kumar and Santhi, 2012). The plant parts were used in treating various diseases such as eczema, fever, ulcer, glandular swellings, digestive disorders, rheumatic disease, dysentery (Ravikumar *et al*., 2012) The antiplasmodial activity and antimicrobial activity of *M. pubescens* were studied by Goyal *et al*., 2013. The plant has high nutritive value (Anuradha *et al*., 2013) and hepatoprotective activity (Jayapal *et al*., 2014). Alkaloids, phenolic compounds, flavonoids, phytosterols, and triterpenes are found in the leaves of *M. pubescens* (Deepti *et al*., 2012). Studies on endophytic bacteria prevailing in this plant have not yet been reported; this paves the way for the present research.